

PATENT
Docket no. 1173-1061PUS3

IN THE U.S. PATENT AND TRADEMARK OFFICE

Applicant: Peter L. COLLINS et al.

Conf. No.: 5376

Appl. No.: 10/789, 400

Art Unit: 1632

Filed: February 27, 2004

Examiner: Shin-Lin Chen

For: RECOMBINANT HUMAN METAPNEUMOVIRUS AND ITS USE

DECLARATION UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Sir:

I, Dr. Peter Collins, hereby declare as follows:

1. I am a U.S. citizen, residing at 2921 Woodstock Avenue, Silver Spring, MD 20910.
2. I am presently employed as Senior Investigator at the National Institutes of Allergy and Infectious Diseases of the National Institutes of Health. A copy of my Curriculum Vitae is attached.
3. I am a co-inventor of the subject matter of the above-identified U.S. Patent application. I am familiar with the specification and pending claims, and with the prosecution history of the application.
4. The Examiner has rejected claims 1-4, 6-8, 15, 16, 18, 25 55 and 56 of the application as being obvious in view of Bermingham et al., *Proc. Natl. Acad. Sci. USA*, 96:11259-11264 (1999)

in view of Van den Hoogen et al., *Nature Medicine* 7:719-714 (2001) and Van den Hoogen et al., *Virology* 295:119-132 (2002).

5. The Examiner asserts that Bermingham teaches the NdeI and K5 mutations, and a few others, that together are made to ablate expression of the M2 ORF2 of HRSV. The Examiner notes that Bermingham use a “minigenome” comprising a Chloramphenicol Amino-Transferase (“CAT”) gene under control of RSV transcription and termination signals to direct synthesis of CAT in the presence of RSV N, P and L proteins, thus as an indirect measure of RSV viral growth in culture. Bermingham et al. are also described as showing that virus lacking M2-2 protein grew less efficiently in vitro and that the authors conclude that the M2-2 protein functions to switch the virus state between one of transcription of viral genes to replication of the viral genome.

6. The Van den Hoogen (2001) paper is cited as teaching the sequence of HMPV, an element necessary to provide enablement of the present invention and plainly lacking from the disclosure of Bermingham, which is directed to a virus distinct from HMPV.

7. The Van den Hoogen (2002) paper is cited as teaching that HMPV infection is a significant clinical problem, causes clinical symptoms similar to RSV, and like RSV is a member of the Pneumovirinae subfamily.

8. The Examiner concludes that one of ordinary skill in the art would have found it obvious, that is, a mere application of ordinary technical skill, to construct a recombinant HMPV or an expression vector having a partial or complete HMPV genome or antigenome comprising one or more attenuating modifications (as in claim 1 as filed), with a reasonable expectation of success in obtaining the present invention.

9. To the contrary, achieving the present invention required considerable inventive activity over what had been disclosed by Bermingham and Van den Hoogen.

10. Whereas RSV viruses can be recovered by reverse genetics methods and propagated in a wide number of cells of human, hamster, bovine, and simian origin, HMPV appears to replicate well only in two lines, namely African green monkey Vero cells and Rhesus monkey LLC-MK2 cells. This is unexpected and unexplained. Furthermore, HMPV replicates much more slowly than RSV, with an infectious cycle of 72-96 h or more compared to 24-48h for RSV. Final yields are reduced by approximately 10-fold or more, which further complicates studies. It is substantially less cytopathic, making it difficult to monitor growth. HMPV also depends on added trypsin in the medium for growth. Because trypsin is unstable due to self-cleavage and metabolism by the cell monolayer, one must first determine optimal conditions for growth and trypsin addition and re-addition, which vary with cell type. Because of the poor growth of HMPV, we had to develop the rescue system using a construct expressing green fluorescent protein as a living tag to monitor recovery and infection. We also could not use the traditional method of supplying T7 RNA polymerase with a vaccinia virus recombinant. This is because, given the long replication cycle and poor growth of HMPV, the rapidly growing vaccinia virus would kill the cells and preclude recovery. This is true even for attenuated strains such as the vaccinia MVA strain, since they remain very cytopathic compared to HMPV. For that reason, it became necessary to develop an amplification method in which we used an available baby hamster kidney cell line that constitutively produces T7 RNA polymerase for initial infection, and co-culture with susceptible Vero or LLC-MK2 cells. This allowed recovery of recombinant virus despite poor growth in the BHK cells. All of this required considerable experimentation and technical skill to finally achieve reliable recovery of recombinant HMPV from cDNA clones.

11. At the time the invention was made, there were reasons to be skeptical of RSV as an exact model for HMPV. The two viruses have been classified in different taxonomic genera, which is an unambiguous scientific determination that the viruses are substantially different. RSV has two additional genes (NS1 and NS2) compared to HMPV. There are some proteins that seem to be similar between the two viruses. However, the most similar ones (such as the

nucleocapsid protein N, phosphoprotein P, matrix protein M, and polymerase protein L) are present in a very wide array of viruses spanning four or more virus families involving widely different viral species. Thus, the presence of proteins bearing the same name is not necessarily indicative of close structural similarity or predictability of function. In addition to lacking the NS1 and NS2 proteins of RSV, HMPV has a different gene order for four of its eight genes compared to RSV. Since gene order is the single most conserved feature of the nonsegmented negative strand RNA viruses, this is indicative of significant difference between RSV and HMPV. Also while the disease caused by HMPV has some similarities to that of RSV, the virus infects later in infancy than RSV and elicits a very different host cytokine response.

12. Between HMPV and RSV, there is 36% amino acid identity between the two putative M2-1 proteins. This is a fairly low value, but the two proteins also share a cysteine-histidine motif that, for RSV, was shown to be important for M2-1 function. In contrast, there is only 12% identity for the two M2-2 proteins and an absence of any shared motif or conserved segment. A value of 12% is insignificant in the absence of conserved motifs, and hence there is no relatedness at all in M2-2 between HMPV and RSV. The M2-1 protein is essential for RSV replication: its deletion is lethal. However, even though M2-1 of HMPV has significant sequence relatedness with that of RSV, and shares a cysteine-histidine motif, we found that it was not essential for replication of HMPV. Specifically, HMPV from which the M2-1 coding sequence had been deleted replicated nearly as efficiently as wild type in cell culture. In addition, HMPV lacking both M2-1 and M2-2 replicated nearly as efficiently as wild type HMPV in cell culture. Thus, deletion of the M2-1 protein, which seems to be related between RSV and HMPV and in particular has a conserved cysteine-histidine motif known to be important for function in RSV, yielded results that were completely different than expectations. Since M2-2 had no sequence relatedness between the two viruses, and further given the contrarian results with M2-1, it would not be reasonable to be able to expect that results related to M2-2 of RSV could be extrapolated to HMPV. That is to say, contrary to the assertion of the Examiner that one who read Bermingham et al. would expect that elimination of the M2-2 protein expression from HMPV

would provide an attenuated HMPV, this is not so, and this is evidence of unobviousness of the present invention.

In other words, the contrarian results obtained with the M2-1 protein illustrate that RSV and HMPV are significantly different – consistent with their classification into different genera – and demonstrate that one cannot rely on a low level of sequence relatedness or other vague similarities to make predictions between viruses from different taxonomic groups.

13. Other aspects of HMPV biology have proven to be different from RSV. For example, with RSV, the attachment G protein is a major neutralization and protective antigen, and is essential for replication in mice. In contrast, for HMPV, the G attachment protein is not a significant attachment or neutralization antigen and is not essential for replication in mice or in non-human primates. Furthermore, whereas RSV G has sequence relatedness to the CX3C chemokine called fractalkine, and mimics its chemotactic activity in vitro, there is no such sequence relatedness between HMPV G and any chemokine. In addition, the RSV G protein is expressed abundantly as a secreted form in addition to the membrane-anchored form. This secreted form functions as an antibody decoy to help the virus evade neutralizing antibodies and also shifts the polarization of T helper cells. Whereas the secreted form of G plays a central role in RSV biology, there is no known secreted form of HMPV G. This is another example involving a protein that seems somewhat similar between RSV and HMPV, but which turns out to have substantial functional differences and for which the effect of deletion is very different. In particular, the finding that G is a neutralization antigen for one virus (RSV) but not the other (HMPV) and is essential for detectable replication in vivo by one virus (RSV) but is dispensable and a useful method of attenuation for the other (HMPV) are major differences that substantially impact vaccine design. In this regard, if one assumed that RSV was a predictive model, one would have emphasized the use of G protein in any vaccine (and indeed at least commercial company has based an experimental RSV vaccine solely on G). Obviously, this presumption would have been calamitous for an HMPV vaccine program. This illustrates why experienced workers in the field

recognize the need to evaluate each attenuating mutation made in HMPV as being novel.

14. At the present time, the M2-2 deletion in HMPV and RSV has some similarities but, also has differences. Both yield viable virus. However, the kinetics of replication in vitro of the RSV M2-2 deletion mutant were substantially reduced compared to wild type RSV, whereas the efficiency of replication of the HMPV M2-2 deletion mutant was the same or greater than that of wild type HMPV in Vero cells (that lack the type I interferon genes). That would be a very unexpected result for one anticipating that RSV would be an accurate predictive model for HMPV, and might suggest that the M2-2 deletion was not attenuating in HMPV. Transcription seems to be up-regulated in both viruses following deletion of M2-2. However, whereas the M2-2 deletion RSV has a decrease in RNA replication associated with the increase in transcription, there does not seem to be a decrease in RNA replication with HMPV. This indicates that the mechanism of the effect is not identical. In addition, there may be a slightly higher level of point mutations with deletion of M2-2 in HMPV compared with RSV, in particular ones in runs of A's and T's. Thus, M2-2 might have an effect on the fidelity of RNA synthesis for HMPV but not RSV. There also is preliminary evidence that M2-2 is an interferon antagonist in HMPV but not RSV (which has these functions in the NS1 and NS2 proteins that HMPV lacks). If so, this would be an important difference between an M2-2 deletion virus in HMPV versus RSV, since interferon affects immunogenicity in a positive way. In practical terms, clinical results and regulatory evaluation of an RSV vaccine based on deletion of M2-2 will not be considered in any way predictive of or relevant to an HMPV vaccine based on deletion of M2-2, given the differences between the viruses and the lack of confidence in extrapolations made across viral genera.

15. Although a partial HMPV sequence was available, this is insufficient to design recombinant virus or to develop vaccine strategies. As mentioned above, the partial sequence provided by Van den Hoogen did not necessarily contain all of the HMPV genes. The sequence provided by Van den Hoogen in fact lacked the key promoter sequences. It is not an

authenticated, functional sequence, i.e., the sequence that was available had not been confirmed to encode a viable virus. This is essential given the high rate of mutation in RNA viruses. Our invention provides a complete functional sequence encoding a wild type-like virus and thus provides a working copy. In other words, one can construct a clone of that sequence and be assured that it will produce infectious virus. Our invention also establishes which proteins must be expressed in trans for recovery – this complement of proteins turns out to be different from RSV since M2-1 is not needed for HMPV replication. As already noted above, our invention also describes precise methods for recovery.

16. In summary, there are substantial differences in the biology and biochemistry of replication of HMPV compared to RSV. These differences are not known in full, since HMPV is a newly described virus and both viruses continue to be the subject of intense research. However, the differences identified to date are sufficient that the two viruses are classified in different genera. A number of specific and unexpected differences have been noted above. Contrary to the assertion of the Examiner, one of ordinary skill in the art, having before him the teachings of Bermingham regarding RSV and the sequence data and clinical information from Van den Hoogen, would **not** have a reasonable expectation of success in achieving an attenuated HMPV (claim 1) by applying the techniques of Bermingham to HMPV to make a recombinant virus that did not express a functional M2-2 protein. Some of the obstacles involve the lack of a working HMPV model, including the lack of a complete inventory of the genes, the lack of information on the specific functions of the genes, the lack of a complete confirmed sequence, and the lack of methods for recovering this slow growing and fastidious virus by recombinant methods. Other obstacles involve differences, both known and anticipated, between the viruses that preclude direct extrapolation between distinct taxonomic groups. Above, we have given examples of substantial differences in the properties of the M2-1, M2-2, and G proteins and viruses from which these genes have been deleted. Pertinent to the M2 gene, HMPV lacking functional M2-2 protein is not attenuated in cells that do not produce interferon, whereas RSV lacking functional M2-2 protein is highly attenuated in vitro regardless of interferon production. The Examiner is referred to pp. 79-80 of the specification.

This is consistent with function of the M2 proteins of HMPV as interferon antagonists. With regard to M2-1, deletion of this protein from RSV is lethal, consistent with its role as an essential transcription elongation factor. In contrast, deletion of M2-1 from HMPV is only slightly attenuating in vitro and yields a virus that appears to transcribe without impediment. It is clear that one cannot extrapolate between these two viruses. The Examiner's speculation that one could directly apply the knowledge about how to attenuate RSV to HMPV is only that. Absent the teachings of the present specification, there simply was not enough known about HMPV at the time the present invention was made to make attenuated HMPV viruses in a directed, predictable fashion using genetic engineering methods.

17. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: 11/09/07 By Peter Cen
(Dr. Peter Collins)

CURRICULUM VITAE**Name:** Peter L. Collins, Ph.D.**Date and Place of Birth:** June 16, 1953; New Haven, Connecticut**Citizenship:** United States**Address:** Home: 2921 Woodstock Avenue
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phone: (301) 594-1590**e-mail:** pcollins@niaid.nih.gov**Education:**

1976	B.S. (Biology), University of Connecticut
1981	Ph.D. (Microbiology), University of Connecticut

Brief Chronology of Employment:

1976 - 1981	Predoctoral Fellow, Microbiology Section, Biological Sciences Group, University of Connecticut, Laboratories of Dr. L. Andrew Ball and Dr. Lawrence E. Hightower.
1981 - 1984	Postdoctoral Fellow, Department of Microbiology and Immunology, University of North Carolina School of Medicine, Laboratory of Dr. Gail W. Wertz
1984 - 1991	Senior Staff Fellow, Public Health Service, Respiratory Viruses Section, Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD
1991 - Present	Senior Investigator, Respiratory Viruses Section, Laboratory of Infectious Diseases, National Institute of

Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD

Professional Societies/Memberships:

American Society for Virology
American Society for Microbiology

Honors and Other Scientific Recognition:

Undergraduate:	State of Connecticut Scholar, Honors Scholar, Phi Beta Kappa, Faculty Scholar, University Scholar (degree <i>Summa Cum Laude</i> , 1976)
Graduate:	National Science Foundation Graduate Fellowship, National Institutes of Health Predoctoral Training Grant, GMO7219 (Individual Grant)
1981 - 1982	National Institutes of Health, Postdoctoral Fellowship, 5 F32 CAO9156-07 (Institutional Training Grant)
1982 - 1984	National Institutes of Health, Postdoctoral Fellowship, 1 F32 A106956-01 (Individual Grant)
1984	Invited instructor, Carolina Biotechnology Workshops
1986	Invited speaker, WHO Respiratory Syncytial and Parainfluenza Viruses Workshops
1986	Invited speaker, Gene Transfer and Expression Conference, Chapel Hill, North Carolina
1987	Workshop chairman, American Society for Virology
1987	Invited symposium speaker, VII International Congress for Virology
1987	Two-week training in the synthesis of synthetic peptides in the laboratory of Dr. Richard Houghten at Scripps Research Institute
1989 - Present	International Committee on Taxonomy of Viruses, Study Group on Paramyxoviridae
1990	Invited speaker, Animal Models of Respiratory Syncytial Virus Infections, Annecy, France

- 1991 Invited speaker, International Meetings on Biology:
 Workshop on Transcription and Replication of Negative
 Strand RNA Viruses, Madrid, Spain
- 1992 Invited session chairman to *Modern Approaches to
Vaccines Including Prevention of Aids*, Cold Spring
 Harbor, New York
- 1993 Invited speaker and session chairman to the Juan March
 Foundation meeting *Reverse Genetics of Negative Stranded
RNA Viruses* in Madrid
- 1993 Invited workshop chairman to the Ninth International
 Congress on Virology, August, 1993
- 1995 Invited Speaker, Research Triangle Virology, Chapel Hill,
 NC
- 1995 NIH Director's Award
- 1996 State of the Art Speaker, American Society for Virology.
- 1996 Keynote Speaker, European Union Third Biotechnology
 Meeting (Madrid).
- 1996 Workshop Chair, NIH Research Festival
- 1996-2003 Principal Investigator, CRADA entitled *Production and
characterization of live attenuated RSV and PIV vaccine
viruses with recombinant DNA* with Wyeth-Lederle
 Biologicals.
- 1996-1999 Co-president, NIH Virology Interest Group, 1996-1999.
- 1996 NIAID Director's Award
- 1997-2000 Co-investigator for a Civilian Research and Development
 Foundation Grant application with Dr. Sergey Netesov of
 the Vektor Laboratory, Novosibirsk, Russia
- 1997 Invited Speaker, *Frontiers of RNA Virus Research*, Kyoto,
 Japan
- 1997 Invited Speaker, *Current Aspects of Vaccinology and
Molecular Virology* Dana Point, CA

- 1997 Member, Search Committee for Branch Chief, I Institute for Dental Research
- 1997 Invited Speaker, *Molecular Approaches to Vaccines*, Bethesda
- 1998 Invited Speaker, *Colloque International Vaccinologie*, l'Academie des Sciences et la Fondation Marcel Merieux
- 1999 Invited Speaker, Keystone Symposium on Viral Vaccines
- 1999 Invited Speaker, *Host and Viral Factors in Viral Infectivity and Pathogenicity*. Tokyo, Japan
- 1999 Invited Speaker, Argentine Congress of Virology, Buenos Aires
- 1999 Keynote speaker, "RSV after 43 Years", Indian River, FL.
- 2000 Chair-elect, RNA viruses Division of the American Society of Microbiology
- 2000 Invited Speaker, *United States Civilian Research and Development Foundation for the Independent States of the Former Soviet Union Symposium 2000*, Moscow
- 2000 Session chair, Negative Strand Viruses 2000, Quebec City
- 2000 Recipient of the Hugh Clark Distinguished Lectorship Award, University of Connecticut
- 2000 Recipient of Yamanouchi USA Foundation research award
- 2000-present Reviewer, NIH Intramural AIDS Targeted Anti-viral Program
- 2001 Colloquium organizer, "Live engineered vaccines", for the 2001 American Society of Microbiology General Meeting, Orlando, FL
- 2001 Two keynote addresses at "RSV after 45 Years", Segovia, Spain.
- 2002 American Society for Microbiology Division T (RNA Viruses) Chairman

2002	Organizing committee: "Workshop on new approaches for human studies to accelerate the development of a safe and effective vaccine to prevent respiratory syncytial disease"
2002	Invited speaker, Juan March Foundation Meeting "Negative strand viral vectors"
2003	Invited plenary lecturer, Society for General Microbiology
2003	Instructor, United States Patent and Trademark Office Technology Fair
2003	Invited speaker, American Pediatric Society Annual Meeting
2003	Invited speaker, "RSV after 47 years", Stone Mountain, Georgia
2004	Session Chair, Workshop on Replication and Cell Biology of Negative Strand RNA Viruses
2005	Invited speaker, Airway Responses to Respiratory Viruses
2005	Invited speaker, NIH Research Festival
2005	Invited speaker and session chair, 2005 Respiratory Syncytial Virus Meeting, Cambridge, United Kingdom
2005	NIAID Merit Award
2006	Ad hoc reviewer for the NIAID Extramural Program
2006	Trans-NIH Research Initiative Planning Committee
2007	Invited speaker and session chair, New Cells for Vaccines

Editorial Boards

Journal of Virology	1989 – 1998, and 2003 - present
Virology	1998 – present
Journal of General Virology	1992 - 1996
Virus Research	2002 – present

Academic Activities

1986	Chairman, Ph.D. thesis committee for Robert C. Jambou, University of Maryland
1993	Outside examiner, Ph.D. thesis committee, K. H. Park, Mount Sinai School of Medicine
1994-2002	Ad hoc co-instructor in graduate virology courses, University of Maryland and Uniformed Services University
1994-1997	Adjunct Assistant Professor, University of Maryland
1994	Outside examiner, Ph.D. thesis committee for Tina M. Meyers, University of Florida
1997-1998	Adjunct Associate Professor, University of Maryland at College Park
1998-2006	Adjunct Professor, University of Maryland at College Park (terminated to avoid conflict of interest issues)
1995-1998	Ph.D. thesis committee for Manoj K. Pastey, University of Maryland
1998-2000	Ph. D. thesis committee for Yunus S. Abdul, University of Maryland
1998-2003	Ph.D. thesis committee for Zhuhui Huang, University of Maryland
2002-2005	Ph.D. thesis committee for Govindarajan Dhanasekaran, University of Maryland

Previous Postdoctoral Trainees

Melaine K. Spriggs, retired from Department of Molecular Biology, Immunex Corp.
(now Amgen, Inc.), Seattle, WA

Robert A. Olmsted, Vice President of Research, AlphaVax, Inc. Research Triangle Park,
NC

Philip R. Johnson, Chief Scientific Officer and Senior Vice President for Research at the
Children's Hospital of Philadelphia

David S. Stec, Associate in the Biotechnology Patent Group of Dorsey, Dorsey and
Whitney LLP, San Francisco, CA

Michael Mink, Scientist, Trimeris, Inc. Durham, NC

Geoffrey Cole, NIAID Extramural Administration, Bethesda, MD

Lili Kuo, Scientist, New York State Department of Health, Albany, NY

Prabha Atreya, CBER, FDA, Bethesda, MD

Rachel Fearn, Assistant Professor, University of Dundee, UK

Michael N. Teng, Assistant Professor, Penn State University, PA

Christine D. Kreml, Research Assistant Professor, Institute for Medicine, Freiburg, Germany

Alison Bermingham, Tenured Scientist, Central Public Health Laboratory, London, UK

Kirsten Spann, Respiratory Virus Research Unit Head, University of Queensland and Sir Albert Sakzewski Virus Research Center, Queensland, Australia

Stephane Biacchesi, Tenured Scientist and Group Leader, Unit of Molecular Virology and Immunology, INRA, Paris, France

Previous Sabbatical Professors

Kenneth Dimock, University of Ottawa, Ottawa, Canada

Haim Grosfeld, Israel Institute for Biological Research, Ness-Ziona, Israel

Juan Cristina, University of the Republic, Montevideo, Uruguay

Siba K. Samal, Virginia-Maryland Regional College of Veterinary Medicine, College Park, MD

Mark E. Peeples, Columbus Children's Research Institute, Columbus OH

Patents

1. Title: Vaccines for human respiratory syncytial virus
Inventors: Peter L. Collins and Gail W. Wertz
Number: 5,149,650
Issued: 09/22/92

2. Title: Human respiratory syncytial virus preparations and processes

Inventors: Peter L. Collins and Gail W. Wertz
Number: 5,716,832
Issued: 02/10/98

3. Title: Production of attenuated respiratory syncytial virus vaccines from cloned nucleotide sequences
Inventors: Brian R. Murphy, Peter L. Collins, Stephen S. Whitehead, Alexander A. Bukreyev, Katalin Juhasz, Michael N. Teng
Number: 5,993,824
Issued: 11/30/99

4. Title: Production of infectious respiratory syncytial virus from cloned nucleotide sequences
Inventor: Peter L. Collins
Number: 6,264,957
Issued: 07/24/01

5. Title: Detection of negative-strand RNA viruses
Inventors: Paul D. Olivo, Sondra Schlesinger, Mark E. Peebles, and Peter L. Collins
Number: 6,270,958
Issued: 08/07/01

6. Title: Recombinant parainfluenza virus vaccines attenuated by deletion or ablation of a non-essential gene
Inventors: Anna P. Durbin, Peter L. Collins and Brian R. Murphy
Number: 6,410,023
Issued: 06/25/02

7. Title: Production of attenuated chimeric respiratory syncytial virus vaccines from cloned nucleotide sequences.
Inventors: Peter Collins, Brian Murphy and Stephen Whitehead
Number: 6,689,367
Issued: 02/10/04

8. Title: Production of recombinant respiratory syncytial viruses expressing immunomodulatory molecules
Inventors: Peter Collins, Alexander Bukreyev, Brian Murphy and Stephen Whitehead
Number: 6,699,476
Issued: 03/02/04

9. Title: Production of attenuated respiratory syncytial virus vaccines involving modification of M2 ORF2
Inventors: Peter Collins, Brian Murphy and Alison Bermingham
Number: 6,713,066
Issued: 03/30/04

10. Title: Methods for producing self-replicating RSV particles comprising recombinant RSV genomes or antigenomes and the N, P, L, and M2 proteins
Inventor: Peter L. Collins
Number: 6,790,449
Issued: 09/14/04
11. Title: Respiratory syncytial virus vaccines expressing protective antigens from promoter-proximal genes
Inventors: Christine D. Kreml, Peter L. Collins, Brian R. Murphy, Ursula J. Buchholz, and Stephen S. Whitehead
Number: 6,923,971
Issued: 08/02/05
12. Title: Use of recombinant parainfluenza viruses (PIVs) as vectors to protect against infection and disease caused by PIV and other human pathogens
Inventors: Brian R. Murphy, Peter L. Collins, Alexander C. Schmidt, Anna P. Durbin, Mario H. Skiadopoulos, and Tao Tao
Number: 7,192,593
Issued: 03/20/07
13. Title: Attenuated human-bovine chimeric parainfluenza virus (PIV) vaccines
Inventors: Alexander C. Schmidt, Mario H. Skiadopoulos, Peter L. Collins, Brian R. Murphy, Jane E. Bailey, Peter L. Collins, Anna P. Durbin
Number: 7,201,907
Issued: 04/10/07
14. Title: Production of attenuated parainfluenza virus vaccines from cloned nucleotides sequences
Inventors: Brian R. Murphy, Peter L. Collins, Anna P. Durbin, Mario H. Skiadopoulos, and Tao Tao
Number : 7,208,161
Issued: 04/24/07
15. Title: Production of novel Newcastle disease virus strains from cDNAs and improved live attenuated Newcastle disease vaccines
Inventors: Siba Samal and Peter Collins
Number: 7,244,558
Issued: 07/17/07
- Title: Paramyxoviruses as gene transfer vectors to lung cells
Inventors: Raymond Pickles, Liqun Zhang, Mark Peeples, Peter Collins and John Olsen
Filed: 9/27/02

Title: Recovery of recombinant human parainfluenza virus type 1 (HPIV1) from cDNA and use of recombinant HPIV1 in immunogenic compositions and as vectors to elicit immune responses against PIV and other human pathogens
Inventors: Brian R. Murphy, Peter L. Collins, Mario H. Skiadopoulos and Jason T. Newman
Filed: 11/21/02

Title: Recovery of recombinant human parainfluenza virus type 2 (HPIV2) from cDNA and use of recombinant HPIV2 as vaccines and vectors to protect against infection and disease caused by PIV and other human pathogens
Inventors: Mario H. Skiadopoulos, Brian R. Murphy, and Peter L. Collins
Filed: 09/18/03

Title: Production of attenuated human-bovine chimeric respiratory syncytial virus vaccines
Inventors: Ursula J. Buchholz, Peter L. Collins, Brian R. Murphy and Stephen S. Whitehead
Filed: 06/23/00

Title: Recombinant metapneumovirus and its use
Inventors: Peter Collins, Stephane Biacchesi, Ursula Buchholz, Brian Murphy and Mario Skiadopoulos
Filed: 2/28/03

Title: Attenuated human parainfluenza virus, methods and uses thereof
Inventors: Sheila Nolan, Mario Skiadopoulos, Peter Collins and Brian Murphy

BIBLIOGRAPHY

- Ph.D. Dissertation: Collins PL. Synthesis and translation of the messenger RNAs of Newcastle disease virus. 1981. Dr. L. Andrew Ball, advisor.
1. Ball LA, White CN, Collins PL. Transcription map of vesicular stomatitis virus. In Baltimore D, Huang AS, Fox CF, eds. *Animal Virology*. New York: Academic Press 1976; pp 419-438.
 2. Collins PL, Hightower LE, Ball LA. Transcription and translation of Newcastle disease virus mRNAs *in vitro*. *J Virol* 1978; **28**:324-336.
 3. Ball LA, Collins PL, Hightower LE. Transcription, translation and mapping of the genes of Newcastle disease virus. In Mahy BWJ, Barry RD (eds.) *Negative Strand Viruses and the Host Cell*. London: Academic Press 1978; pp 395-405.
 4. Collins PL, Hightower LE, Ball LA. Transcriptional map for Newcastle disease virus. *J Virol* 1980; **35**:682-693.
 5. Collins PL, Wertz GTW, Ball LA, Hightower LE. Translation of the separated messenger RNAs of Newcastle disease virus. In Bishop DHL, Compans RW (eds.) *Replication of Negative Strand Viruses*. New York: Elsevier-North Holland 1981; pp 535-543.
 6. Collins PL, Fuller FJ, Marcus PI, Hightower LE, Ball LA. Synthesis and processing of Sindbis virus nonstructural proteins *in vitro*. *Virology* 1982; **118**:367-379.
 7. Collins PL, Wertz GW, Ball LA, Hightower LE. Coding assignments of the five smaller mRNAs of Newcastle disease virus. *J Virol* 1982; **43**:1024-1031.
 8. Collins PL, Hightower LE. Newcastle disease virus stimulates the cellular accumulation of stress (heat shock) mRNAs and proteins. *J Virol* 1982; **44**:703-707.
 9. Collins PL, Wertz GW. cDNA cloning and transcriptional mapping of nine polyadenylated RNAs encoded by the genome of human respiratory syncytial virus. *Proc Natl Acad Sci USA* 1983; **80**:3208-3212.
 10. Collins PL, Huang YT, Wertz GW. Identification of a tenth mRNA for respiratory syncytial virus and assignment of polypeptides to the ten viral genes. *J Virol* 1983; **49**:572-578.
 11. Collins PL, Dickens LE, Wertz GW. cDNA cloning, mapping and translation of ten respiratory syncytial virus genes. In Bishop DHL, Compans RW (eds.)

- Molecular Biology of Negative Strand Viruses.* New York: Academic Press 1984; pp 21-26.
12. Collins PL, Huang YT, Wertz GW. Nucleotide sequence of the gene encoding the fusion (F) glycoprotein of human respiratory syncytial virus. *Proc Natl Acad Sci USA* 1984;**81**:7683-7687.
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246. Di Napoli JM, Kotelkin A, Yang L, Elankumaran A, Murphy BR, Samal SK, Collins PL, Bukreyev A. Newcastle disease virus, a highly host-range-restricted virus, as a vaccine vector against emerging pathogens *Proc Natl Acad Sci USA* 2007; 104:9788-9793. *

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 255. Collins PL and Graham BS. Viral and host factors in human respiratory syncytial virus pathogenesis. *J Virol* *
- * *Invited Mini-review*
256. Bukreyev A and Collins PL. Advances in the development of vaccines against Marburg and Ebola viruses *Future Virology*
 257. Vallbracht S, Jessen B, Mrusek S, Enders A, Collins PL, Ehl S, Kreml CD. A single viral epitope determines T cell response and disease after infection of mice with respiratory syncytial virus. *J Immunol*

CURRICULUM VITAE

Name: Peter L. Collins, Ph.D.

Date and Place of Birth: June 16, 1953; New Haven, Connecticut

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Education:

1976 B.S. (Biology), University of Connecticut
1981 Ph.D. (Microbiology), University of Connecticut

Brief Chronology of Employment:

1976 - 1981 Predoctoral Fellow, Microbiology Section, Biological Sciences Group, University of Connecticut, Laboratories of Dr. L. Andrew Ball and Dr. Lawrence E. Hightower.

1981 - 1984 Postdoctoral Fellow, Department of Microbiology and Immunology, University of North Carolina School of Medicine, Laboratory of Dr. Gail W. Wertz

1984 - 1991 Senior Staff Fellow, Public Health Service, Respiratory Viruses Section, Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD

1991 -Present Senior Investigator, Respiratory Viruses Section,
Laboratory of Infectious Diseases, National Institute of

Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD

Professional Societies/Memberships:

American Society for Virology
American Society for Microbiology

Honors and Other Scientific Recognition:

Undergraduate:	State of Connecticut Scholar, Honors Scholar, Phi Beta Kappa, Faculty Scholar, University Scholar (degree <i>Summa Cum Laude</i> , 1976)
Graduate:	National Science Foundation Graduate Fellowship, National Institutes of Health Predoctoral Training Grant, GMO7219 (Individual Grant)
1981 - 1982	National Institutes of Health, Postdoctoral Fellowship, 5 F32 CAO9156-07 (Institutional Training Grant)
1982 - 1984	National Institutes of Health, Postdoctoral Fellowship, 1 F32 A106956-01 (Individual Grant)
1984	Invited instructor, Carolina Biotechnology Workshops
1986	Invited speaker, WHO Respiratory Syncytial and Parainfluenza Viruses Workshops
1986	Invited speaker, Gene Transfer and Expression Conference, Chapel Hill, North Carolina
1987	Workshop chairman, American Society for Virology
1987	Invited symposium speaker, VII International Congress for Virology
1987	Two-week training in the synthesis of synthetic peptides in the laboratory of Dr. Richard Houghten at Scripps Research Institute
1989 - Present	International Committee on Taxonomy of Viruses, Study Group on Paramyxoviridae
1990	Invited speaker, Animal Models of Respiratory Syncytial Virus Infections, Annecy, France

- 1991 Invited speaker, International Meetings on Biology:
 Workshop on Transcription and Replication of Negative
 Strand RNA Viruses, Madrid, Spain
- 1992 Invited session chairman to *Modern Approaches to
Vaccines Including Prevention of Aids*, Cold Spring
 Harbor, New York
- 1993 Invited speaker and session chairman to the Juan March
 Foundation meeting *Reverse Genetics of Negative Stranded
RNA Viruses* in Madrid
- 1993 Invited workshop chairman to the Ninth International
 Congress on Virology, August, 1993
- 1995 Invited Speaker, Research Triangle Virology, Chapel Hill,
 NC
- 1995 NIH Director's Award
- 1996 State of the Art Speaker, American Society for Virology.
- 1996 Keynote Speaker, European Union Third Biotechnology
 Meeting (Madrid).
- 1996 Workshop Chair, NIH Research Festival
- 1996-2003 Principal Investigator, CRADA entitled *Production and
characterization of live attenuated RSV and PIV vaccine
viruses with recombinant DNA* with Wyeth-Lederle
 Biologicals.
- 1996-1998 Co-president, NIH Virology Interest Group, 1996-1999.
- 1996 NIAID Director's Award
- 1997-2000 Co-investigator for a Civilian Research and Development
 Foundation Grant application with Dr. Sergey Netesov of
 the Vektor Laboratory, Novosibirsk, Russia
- 1997 Invited Speaker, *Frontiers of RNA Virus Research*, Kyoto,
 Japan
- 1997 Invited Speaker, *Current Aspects of Vaccinology and
Molecular Virology* Dana Point, CA

1997	Member, Search Committee for Branch Chief, I Institute for Dental Research
1997	Invited Speaker, <i>Molecular Approaches to Vaccines</i> , Bethesda
1998	Invited Speaker, <i>Colloque International Vaccinologie</i> , l'Academie des Sciences et la Fondation Marcel Merieux
1999	Invited Speaker, Keystone Symposium on Viral Vaccines
1999	Invited Speaker, <i>Host and Viral Factors in Viral Infectivity and Pathogenicity</i> . Tokyo, Japan
1999	Invited Speaker, Argentine Congress of Virology, Buenos Aires
1999	Keynote speaker, "RSV after 43 Years", Indian River, FL.
2000	Chair-elect, RNA viruses Division of the American Society of Microbiology
2000	Invited Speaker, <i>United States Civilian Research and Development Foundation for the Independent States of the Former Soviet Union Symposium 2000</i> , Moscow
2000	Session chair, Negative Strand Viruses 2000, Quebec City
2000	Recipient of the Hugh Clark Distinguished Lectorship Award, University of Connecticut
2000	Recipient of Yamanouchi USA Foundation research award
2000-present	Reviewer, NIH Intramural AIDS Targeted Anti-viral Program
2001	Colloquium organizer, "Live engineered vaccines", for the 2001 American Society of Microbiology General Meeting, Orlando, FL
2001	Two keynote addresses at "RSV after 45 Years", Segovia, Spain.
2002	American Society for Microbiology Division T (RNA Viruses) Chairman

2002	Organizing committee: "Workshop on new approaches for human studies to accelerate the development of a safe and effective vaccine to prevent respiratory syncytial disease"
2002	Invited speaker, Juan March Foundation Meeting "Negative strand viral vectors"
2003	Invited plenary lecturer, Society for General Microbiology
2003	Instructor, United States Patent and Trademark Office Technology Fair
2003	Invited speaker, American Pediatric Society Annual Meeting
2003	Invited speaker, "RSV after 47 years", Stone Mountain, Georgia
2004	Session Chair, Workshop on Replication and Cell Biology of Negative Strand RNA Viruses
2005	Invited speaker, Airway Responses to Respiratory Viruses
2005	Invited speaker, NIH Research Festival
2005	Invited speaker and session chair, 2005 Respiratory Syncytial Virus Meeting, Cambridge, United Kingdom
2005	NIAID Merit Award
2006	Ad hoc reviewer for the NIAID Extramural Program
2006	Trans-NIH Research Initiative Planning Committee
2007	Invited speaker and session chair, New Cells for Vaccines

Editorial Boards

Journal of Virology	1989 – 1998, and 2003 - present
Virology	1998 – present
Journal of General Virology	1992 - 1996
Virus Research	2002 – present

Academic Activities

1986	Chairman, Ph.D. thesis committee for Robert C. Jambou, University of Maryland
1993	Outside examiner, Ph.D. thesis committee, K. H. Park, Mount Sinai School of Medicine
1994-2002	Ad hoc co-instructor in graduate virology courses, University of Maryland and Uniformed Services University
1994-1997	Adjunct Assistant Professor, University of Maryland
1994	Outside examiner, Ph.D. thesis committee for Tina M. Meyers, University of Florida
1997-1998	Adjunct Associate Professor, University of Maryland at College Park
1998-2006	Adjunct Professor, University of Maryland at College Park (terminated to avoid conflict of interest issues)
1995-1998	Ph.D. thesis committee for Manoj K. Pastey, University of Maryland
1998-2000	Ph. D. thesis committee for Yunus S. Abdul, University of Maryland
1998-2003	Ph.D. thesis committee for Zhuhui Huang, University of Maryland
2002-2005	Ph.D. thesis committee for Govindarajan Dhanasekaran, University of Maryland

Previous Postdoctoral Trainees

Melaine K. Spriggs, retired from Department of Molecular Biology, Immunex Corp.
(now Amgen, Inc.), Seattle, WA

Robert A. Olmsted, Vice President of Research, AlphaVax, Inc. Research Triangle Park,
NC

Philip R. Johnson, Chief Scientific Officer and Senior Vice President for Research at the
Children's Hospital of Philadelphia

David S. Stec, Associate in the Biotechnology Patent Group of Dorsey, Dorsey and
Whitney LLP, San Francisco, CA

Michael Mink, Scientist, Trimeris, Inc. Durham, NC

Geoffrey Cole, NIAID Extramural Administration, Bethesda, MD

Lili Kuo, Scientist, New York State Department of Health, Albany, NY

Prabha Atreya, CBER, FDA, Bethesda, MD

Rachel Fearn, Assistant Professor, University of Dundee, UK

Michael N. Teng, Assistant Professor, Penn State University, PA

Christine D. Kreml, Research Assistant Professor, Institute for Medicine, Freiburg, Germany

Alison Bermingham, Tenured Scientist, Central Public Health Laboratory, London, UK

Kirsten Spann, Respiratory Virus Research Unit Head, University of Queensland and Sir Albert Sakzewski Virus Research Center, Queensland, Australia

Stephane Biacchesi, Tenured Scientist and Group Leader, Unit of Molecular Virology and Immunology, INRA, Paris, France

Previous Sabbatical Professors

Kenneth Dimock, University of Ottawa, Ottawa, Canada

Haim Grosfeld, Israel Institute for Biological Research, Ness-Ziona, Israel

Juan Cristina, University of the Republic, Montevideo, Uruguay

Siba K. Samal, Virginia-Maryland Regional College of Veterinary Medicine, College Park, MD

Mark E. Peeples, Columbus Children's Research Institute, Columbus OH

Patents

1. Title: Vaccines for human respiratory syncytial virus
Inventors: Peter L. Collins and Gail W. Wertz
Number: 5,149,650
Issued: 09/22/92

2. Title: Human respiratory syncytial virus preparations and processes

Inventors: Peter L. Collins and Gail W. Wertz
Number: 5,716,832
Issued: 02/10/98

3. Title: Production of attenuated respiratory syncytial virus vaccines from cloned nucleotide sequences
Inventors: Brian R. Murphy, Peter L. Collins, Stephen S. Whitehead, Alexander A. Bukreyev, Katalin Juhasz, Michael N. Teng
Number: 5,993,824
Issued: 11/30/99

4. Title: Production of infectious respiratory syncytial virus from cloned nucleotide sequences
Inventor: Peter L. Collins
Number: 6,264,957
Issued: 07/24/01

5. Title: Detection of negative-strand RNA viruses
Inventors: Paul D. Olivo, Sondra Schlesinger, Mark E. Peebles, and Peter L. Collins
Number: 6,270,958
Issued: 08/07/01

6. Title: Recombinant parainfluenza virus vaccines attenuated by deletion or ablation of a non-essential gene
Inventors: Anna P. Durbin, Peter L. Collins and Brian R. Murphy
Number: 6,410,023
Issued: 06/25/02

7. Title: Production of attenuated chimeric respiratory syncytial virus vaccines from cloned nucleotide sequences.
Inventors: Peter Collins, Brian Murphy and Stephen Whitehead
Number: 6,689,367
Issued: 02/10/04

8. Title: Production of recombinant respiratory syncytial viruses expressing immunomodulatory molecules
Inventors: Peter Collins, Alexander Bukreyev, Brian Murphy and Stephen Whitehead
Number: 6,699,476
Issued: 03/02/04

9. Title: Production of attenuated respiratory syncytial virus vaccines involving modification of M2 ORF2
Inventors: Peter Collins, Brian Murphy and Alison Bermingham
Number: 6,713,066
Issued: 03/30/04

10. Title: Methods for producing self-replicating RSV particles comprising recombinant RSV genomes or antigenomes and the N, P, L, and M2 proteins
Inventor: Peter L. Collins
Number: 6,790,449
Issued: 09/14/04
11. Title: Respiratory syncytial virus vaccines expressing protective antigens from promoter-proximal genes
Inventors: Christine D. Krempel, Peter L. Collins, Brian R. Murphy, Ursula J. Buchholz, and Stephen S. Whitehead
Number: 6,923,971
Issued: 08/02/05
12. Title: Use of recombinant parainfluenza viruses (PIVs) as vectors to protect against infection and disease caused by PIV and other human pathogens
Inventors: Brian R. Murphy, Peter L. Collins, Alexander C. Schmidt, Anna P. Durbin, Mario H. Skiadopoulos, and Tao Tao
Number: 7,192,593
Issued: 03/20/07
13. Title: Attenuated human-bovine chimeric parainfluenza virus (PIV) vaccines
Inventors: Alexander C. Schmidt, Mario H. Skiadopoulos, Peter L. Collins, Brian R. Murphy, Jane E. Bailey, Peter L. Collins, Anna P. Durbin
Number: 7,201,907
Issued: 04/10/07
14. Title: Production of attenuated parainfluenza virus vaccines from cloned nucleotides sequences
Inventors: Brian R. Murphy, Peter L. Collins, Anna P. Durbin, Mario H. Skiadopoulos, and Tao Tao
Number : 7,208,161
Issued: 04/24/07
15. Title: Production of novel Newcastle disease virus strains from cDNAs and improved live attenuated Newcastle disease vaccines
Inventors: Siba Samal and Peter Collins
Number: 7,244,558
Issued: 07/17/07
- Title: Paramyxoviruses as gene transfer vectors to lung cells
Inventors: Raymond Pickles, Liqun Zhang, Mark Peeples, Peter Collins and John Olsen
Filed: 9/27/02

Title: Recovery of recombinant human parainfluenza virus type 1 (HPIV1) from cDNA and use of recombinant HPIV1 in immunogenic compositions and as vectors to elicit immune responses against PIV and other human pathogens
Inventors: Brian R. Murphy, Peter L. Collins, Mario H. Skiadopoulos and Jason T. Newman
Filed: 11/21/02

Title: Recovery of recombinant human parainfluenza virus type 2 (HPIV2) from cDNA and use of recombinant HPIV2 as vaccines and vectors to protect against infection and disease caused by PIV and other human pathogens
Inventors: Mario H. Skiadopoulos, Brian R. Murphy, and Peter L. Collins
Filed: 09/18/03

Title: Production of attenuated human-bovine chimeric respiratory syncytial virus vaccines
Inventors: Ursula J. Buchholz, Peter L. Collins, Brian R. Murphy and Stephen S. Whitehead
Filed: 06/23/00

Title: Recombinant metapneumovirus and its use
Inventors: Peter Collins, Stephane Biacchesi, Ursula Buchholz, Brian Murphy and Mario Skiadopoulos
Filed: 2/28/03

Title: Attenuated human parainfluenza virus, methods and uses thereof
Inventors: Sheila Nolan, Mario Skiadopoulos, Peter Collins and Brian Murphy

BIBLIOGRAPHY

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1. Ball LA, White CN, Collins PL. Transcription map of vesicular stomatitis virus. In Baltimore D, Huang AS, Fox CF, eds. *Animal Virology*. New York: Academic Press 1976; pp 419-438.
 2. Collins PL, Hightower LE, Ball LA. Transcription and translation of Newcastle disease virus mRNAs *in vitro*. *J Virol* 1978; **28**:324-336.
 3. Ball LA, Collins PL, Hightower LE. Transcription, translation and mapping of the genes of Newcastle disease virus. In Mahy BWJ, Barry RD (eds.) *Negative Strand Viruses and the Host Cell*. London: Academic Press 1978; pp 395-405.
 4. Collins PL, Hightower LE, Ball LA. Transcriptional map for Newcastle disease virus. *J Virol* 1980; **35**:682-693.
 5. Collins PL, Wertz GTW, Ball LA, Hightower LE. Translation of the separated messenger RNAs of Newcastle disease virus. In Bishop DHL, Compans RW (eds.) *Replication of Negative Strand Viruses*. New York: Elsevier-North Holland 1981; pp 535-543.
 6. Collins PL, Fuller FJ, Marcus PI, Hightower LE, Ball LA. Synthesis and processing of Sindbis virus nonstructural proteins *in vitro*. *Virology* 1982; **118**:367-379.
 7. Collins PL, Wertz GW, Ball LA, Hightower LE. Coding assignments of the five smaller mRNAs of Newcastle disease virus. *J Virol* 1982; **43**:1024-1031.
 8. Collins PL, Hightower LE. Newcastle disease virus stimulates the cellular accumulation of stress (heat shock) mRNAs and proteins. *J Virol* 1982; **44**:703-707.
 9. Collins PL, Wertz GW. cDNA cloning and transcriptional mapping of nine polyadenylated RNAs encoded by the genome of human respiratory syncytial virus. *Proc Natl Acad Sci USA* 1983; **80**:3208-3212.
 10. Collins PL, Huang YT, Wertz GW. Identification of a tenth mRNA for respiratory syncytial virus and assignment of polypeptides to the ten viral genes. *J Virol* 1983; **49**:572-578.
 11. Collins PL, Dickens LE, Wertz GW. cDNA cloning, mapping and translation of ten respiratory syncytial virus genes. In Bishop DHL, Compans RW (eds.)

- Molecular Biology of Negative Strand Viruses.* New York: Academic Press 1984; pp 21-26.
12. Collins PL, Huang YT, Wertz GW. Nucleotide sequence of the gene encoding the fusion (F) glycoprotein of human respiratory syncytial virus. *Proc Natl Acad Sci USA* 1984;**81**:7683-7687.
 13. Dickens LE, Collins PL, Wertz GW. Transcriptional mapping of respiratory syncytial virus. *J Virol* 1984;**52**:364-369.
 14. Hightower LE, Collins PL, Smith GW. Identification of a phosphorylated nonstructural form of the P protein of Newcastle disease virus and analysis of P multimers. *J Gen Virol* 1984;**65**:1631-1636.
 15. Hightower LE, Smith GW, Collins PL. How many forms of the Newcastle virus P protein are there? In: Bishop DHL, Compans RW (eds.) *Molecular Biology of Negative Strand Viruses.* New York, Academic Press 1984; pp 301-303.
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 17. Collins PL, Anderson K, Langer SJ, Wertz GW. Correct sequence for the major nucleocapsid protein mRNA of respiratory syncytial virus. *Virology* 1985;**146**:69-77.
 18. Collins PL, Wertz GW. Gene products and genome organization of human respiratory syncytial (RS) virus. Cold Spring Harbor Conference, 1984. In Lerner R, Brown F, Chanock R (eds.) *Modern Approaches to Vaccines: Molecular and Chemical Basis of Resistance to Viral, Bacterial and Parasitic Diseases.* New York: Cold Spring Harbor Laboratory 1985; pp 297- 301
 19. Collins PL, Wertz GW. The 1A protein of human respiratory syncytial virus: nucleotide sequence of the mRNA and a related polycistronic transcript. *Virology* 1985;**141**:283-291.
 20. Collins PL, Wertz GW. The envelope-associated 22k dalton protein of human respiratory syncytial virus: nucleotide sequence of the mRNA and a related polytranscript. *J Virol* 1985;**54**:65-71.
 21. Collins PL, Wertz GW. Nucleotide sequence of the 1B and 1C nonstructural protein mRNAs of human respiratory syncytial virus. *Virology* 1985;**143**:442-451.

22. Huang YT, Collins PL, Wertz GW. Characterization of the proteins of human respiratory syncytial virus: identification of a fourth envelope-associated protein. *Virus Research* 1985;2:157-173.
23. Wertz GW, Collins PL, Gruber C, Levine S, Ball LA. Nucleotide sequence of the G protein gene of human respiratory syncytial virus reveals a novel type of viral membrane protein. *Proc Natl Acad Sci USA* 1985;82:4075-4079.
24. Ball LA, Young KKY, Anderson K, Collins PL, Wertz GW. Expression of the major glycoprotein G of human respiratory syncytial virus from recombinant vaccinia virus vectors. *Proc Natl Acad Sci USA* 1986;83:246-250.
25. Collins PL, Dickens LE, Buckler-White A, Olmsted RA, Spriggs MK, Coelingh KVW. Nucleotide sequences for the gene junctions of human respiratory syncytial virus reveal distinctive features of intergenic structure and gene order. *Proc Natl Acad Sci USA* 1986;83:4594-4598.
26. Olmsted RA, Elango N, Prince GA, Murphy BR, Johnson PR, Moss B, Chanock RM, Collins PL. Expression of the F glycoprotein of respiratory syncytial virus by a recombinant virus: comparison of the individual contributions of the F and G glycoproteins to host immunity. *Proc Natl Acad Sci USA* 1986;83:7462-7466.
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28. Spriggs MK, Olmsted RA, Venkatesan S, Coligan JE, Collins PL. Fusion glycoprotein of human parainfluenza virus type 3: nucleotide sequence of the gene, direct identification of the cleavage activation site, and comparison with other paramyxoviruses. *Virology* 1986;152:241-251.
29. Coelingh KL, Winter CC, Murphy BR, Rice JM, Kimball PC, Collins PL. Conserved epitopes on the hemagglutinin-neuraminidase proteins of human and bovine parainfluenza type 3 viruses: nucleotide sequence analysis of variants selected with monoclonal antibodies. *J Virol* 1986;60:90-96.
30. Collins PL, Wertz GW. Human respiratory syncytial virus genome and gene products. In Notkins AL, Oldstone MBA (eds.) *Concepts in Viral Pathogenesis II*. New York: Springer-Verlag 1986; pp 40-46.
31. Jambou RC, Elango N, Venkatesan S, Collins PL. Complete sequence of the major nucleocapsid protein gene of human parainfluenza type 3 virus: comparison with other negative strand viruses. *J Gen Virol* 1986;67:2543-2548.

32. Spriggs MK, Collins PL. Sequence analysis of the P and C protein genes of human parainfluenza virus type 3: patterns of amino acid homology among paramyxoviral proteins. *J Gen Virol* 1986;67:2705-2719.
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41. Coelingh KL, Murphy BR, Collins PL, Lebacq-Verheyden AM, Battey JF. Expression of biologically active and antigenically authentic parainfluenza type 3 virus hemagglutinin-neuraminidase glycoprotein by a recombinant baculovirus. *Virology* 1987;160:465-472.
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